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CASE REPORT

Primary gastric synovial sarcoma

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Synovial sarcoma is a malignant soft tissue neoplasm that may arise from a variety of sites in the human body. It is typically characterized by its biphasic histological pattern, but a monophasic type composed entirely of spindle cells also exists. The diagnosis of monophasic synovial sarcoma can be very challenging and often requires molecular diagnostic techniques, especially for tumors arising in rare locations such as the gastrointestinal tract. We report here the case of a 38-year-old woman with a primary gastric monophasic synovial sarcoma confirmed by reverse transcriptase polymerase chain reaction that revealed t(X;18) (*SYT–SSX1*) translocation. To our knowledge, only 11 synovial sarcomas arising in the stomach have previously been reported. The pathologic features, differential diagnoses, and clinical manifestations are discussed.
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Introduction

Synovial sarcoma is a malignant soft tissue neoplasm traditionally known for its biphasic histological pattern and relatively high rate of occurrence near joints. The nomenclature is, however, actually a misnomer as no evidence of differentiation toward synovium has been found and the tumor can occur in almost any part of the body.[1] Further, many synovial sarcomas are of the monophasic type, composed entirely of spindle cells, and can hardly be associated with synovium in terms of morphology.[1] The diagnosis of monophasic synovial sarcoma often requires ancillary techniques such as immunohistochemical staining and confirmatory molecular studies that reveal t(X;18) resulting in a fusion of *SYT* with *SSX1*, *SSX2*, or rarely *SSX4*.[1,2] Primary gastric synovial sarcomas are extremely rare, only 11 cases having previously been reported in the English-speaking literature.[3,4] Here, we present a case of primary gastric synovial sarcoma and review the related literature.

Case report

A 38-year-old woman presented with recent hunger pain and passage of tarry stools. She had had a history of gastric ulcer for more than 20 years and was receiving intermittent

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medical treatment. Panendoscopy revealed groups of polypoid lesions with ulceration (Fig. 1A). Mucosal biopsy was performed, and histological examination revealed a spindle cell malignancy. A subsequent barium study showed an irregular mass, 7.5 cm in size, in the middle portion of the body of the stomach (Fig. 1B). Abdominal and chest computed tomography (CT) did not reveal any other tumor lesions. There was no any clinical evidence of other possible primary site. The patient underwent wedge resection of the gastric tumor.

The surgical specimen demonstrated a yellow to gray-white, firm mass measuring 7.2 cm × 6.0 cm × 2.7 cm in size, with overlying ulceration (Fig. 2A). Grossly, the tumor involved whole layers of the gastric wall. Microscopically, the gastric tumor was hypercellular and composed of spindle cells containing indistinct cytoplasm and uniform nuclei with delicate to finely granular chromatin. The tumor cells were arranged in long fascicles interlacing at sharp angles and raggedly infiltrating the gastric wall from the mucosa to the serosa (Fig. 2B—2D). Mitotic figures were prominent (> 20 per 10 fields 400×; Fig. 2F). Tumor thrombi were noted in the medium-sized vessels (Fig. 2E). The adjacent omentum also revealed foci of metastatic tumor. In addition, no *Helicobacter pylori* bacilli was found in the gastric mucosa.

Immunohistochemically, the tumor cells were focally reactive to cytokeratin (AE1/AE3) and CD99 (Fig. 2G, 2H). They were negative for c-KIT (despite highlighting intermixed mast cells; Fig. 2I), CD34, discovered on GIST-1 protein (DOG1), cytokeratin 7, smooth muscle actin, estrogen receptor, progesterone receptor, CD10 and Wilms' tumor protein (WT-1). Reverse transcriptase-polymerase chain reaction (RT-PCR) study revealed a chimeric transcript of *SYT—SSX1* fusion gene (Fig. 3A), further confirmed with complementary DNA sequencing (Fig. 3B).

Three months after the operation, follow-up abdominal CT revealed multiple metastatic tumors in the liver (see Fig. 1C). The patient received three courses of chemotherapy (ifosfamide 2000 mg/m^2 and adriamycin 15 mg/m^2 on the first to third days, repeated every 21—28 days). Follow-up CT in the sixth postoperative month showed dramatic shrinkage of the metastatic tumors in the liver (Fig. 1D).

Discussion

Synovial sarcoma is a malignant mesenchymal tumor that tends to arise in the limbs, especially in the vicinity of the knee joints,[1] although it has been encountered in a wide variety of locations, including the internal organs. It was erroneously deemed a tumor of synovial differentiation, probably due to the typically biphasic growth pattern in addition to its usual juxta-articular location.[5] However, monophasic fibrous synovial sarcomas composed exclusively of spindle cells are sometimes encountered,

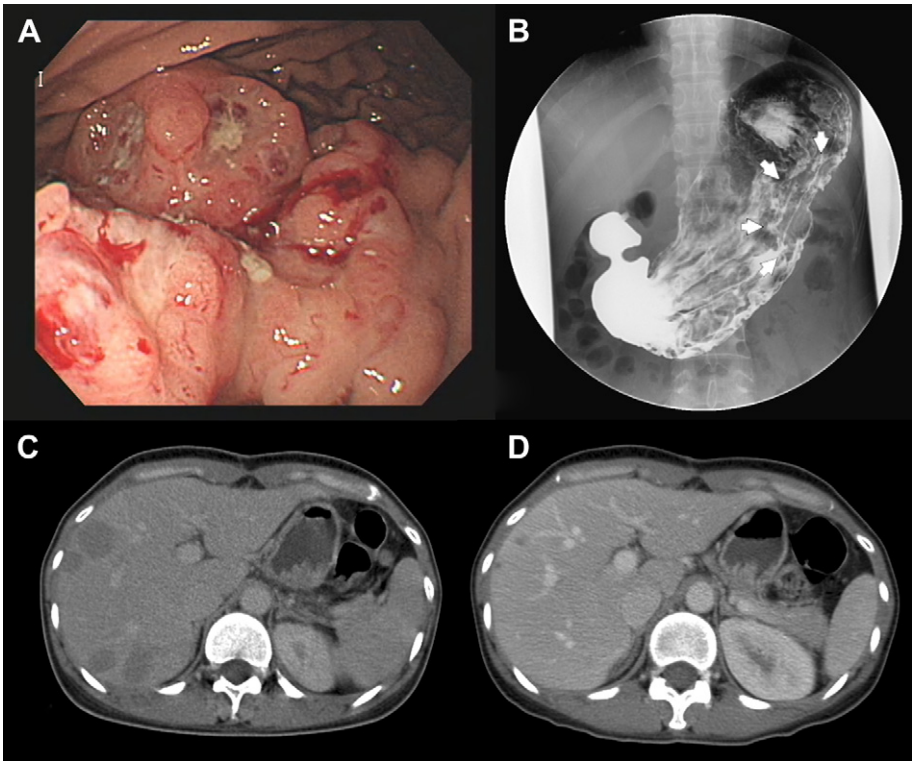

Figure 1 (A) Endoscopic examination revealed a polypoid tumor with a lobulated appearance and ulceration. (B) Barium study showed a mucosal filling defect in the middle portion of gastric body along the greater curvature (arrows). (C) Computed tomography 3 months after surgery revealed multiple hypoenhanced metastatic foci in the right lobe of liver. (D) After three courses of chemotherapy, the metastatic foci significantly decreased in size as shown in follow-up computed tomography at the same level as in C.

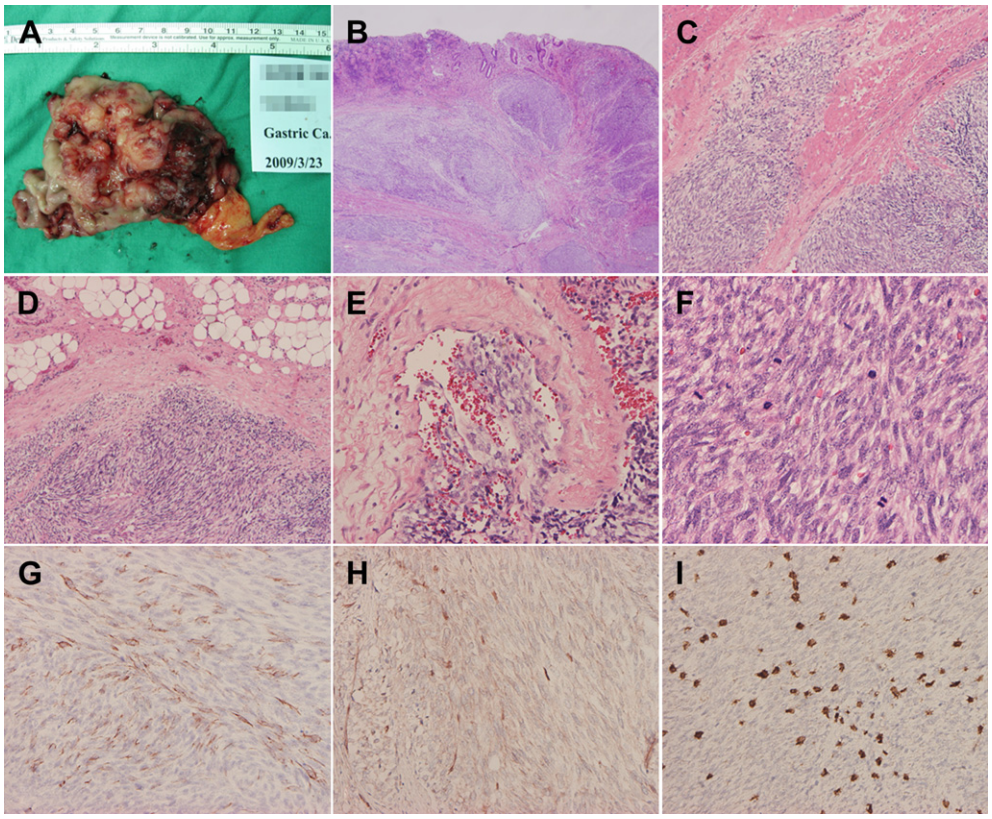

Figure 2 (A) Gross picture of the gastric tumor. (B) The mucosa is involved by the tumor and ulcerated. H&E stain,12.5×. (C) The tumor is invading the gastric wall with an infiltrative border. H&E, 40×. (D) The omental fat is also involved. H&E, 40×. (E) Vascular invasion is present. H&E, 100×. (F) The tumor cells are uniformly spindle-shaped with brisk mitotic figures. H&E, 200×. The tumor cells are focally immunoreactive to cytokeratin (AE1/AE3) (G) and CD99 (H). (I) c-KIT is positive in the scattered mast cells but not the tumor cells.

and these can cause significant diagnostic problems if immunohistochemical or genetic studies are not carried out. Immunohistochemically, synovial sarcomas are often focally reactive to cytokeratins and/or epithelial membrane antigen,[1] evidencing the epithelial differentiation. Immunohistochemistry plays an important and often efficient role in distinguishing synovial sarcomas from tumors that mimic them, although some pitfalls should be kept in mind, as discussed below.

When a pathologist deals with a spindle cell tumor arising in the gastrointestinal tract, gastrointestinal stromal tumors (GIST) usually spring to mind first. These are composed of short spindle and/or epithelioid cells often with vacuolated cytoplasm, sometimes exhibiting nuclear palisading, features that were not seen in the present case. Commonly, one can differentiate a GIST from synovial sarcoma as c-KIT (CD117) is expressed in most GISTs, although c-KIT also stains mast cells, which are often numerous in synovial sarcomas (see Fig. 2I). Leiomyosarcomas and malignant spindle cell melanomas are characterized by a higher degree of pleomorphism, and a panel of smooth muscle markers and melanocytic markers, respectively, can usually confirm the diagnoses. Sarcomatoid carcinoma often exhibits conspicuous pleomorphism and a higher level of epithelial markers, and is usually accompanied by conventional carcinoma. Regardless of the peculiar location, the chief mimickers are malignant peripheral nerve sheath tumor and fibrosarcoma, especially the former in terms of overlapping in immunoprofile.[6–8] Further, synovial sarcoma can occasionally mimic a Ewing's sarcoma or malignant solitary fibrous tumor.[1] In brief, the morphology and immunoprofile can often distinguish these mimickers from synovial sarcomas, but molecular genetic studies may be needed for confirmation in difficult cases.

The unique chromosomal change at t(X;18) with resultant *SYT—SSX* fusion genes is both sensitive and specific to synovial sarcoma, and can be effectively detected in formalin-fixed, paraffin-embedded tissue using RT-PCR.[9,10] As discussed earlier, detection of these translocations is often necessary for the diagnosis of monophasic synovial sarcomas, especially for those arising in unusual sites, perfectly exemplified by the current case.

To date, only 23 cases of primary synovial sarcomas in gastrointestinal tract have been reported in the English literature[3,4,11–14], and 11 of these have arisen in the stomach (Table 1). Nine of the 11 primary gastric tumors and both duodenal tumors were of the monophasic fibrous type, and most of them were confirmed with RT-PCR or fluorescence *in situ* hybridization. These gastrointestinal monophasic synovial sarcomas have been reported in only the past few years, probably reflecting the fact that a wider application of immunohistochemistry and molecular techniques, as well as a growing awareness of the existence of visceral counterparts, has increasingly identified these

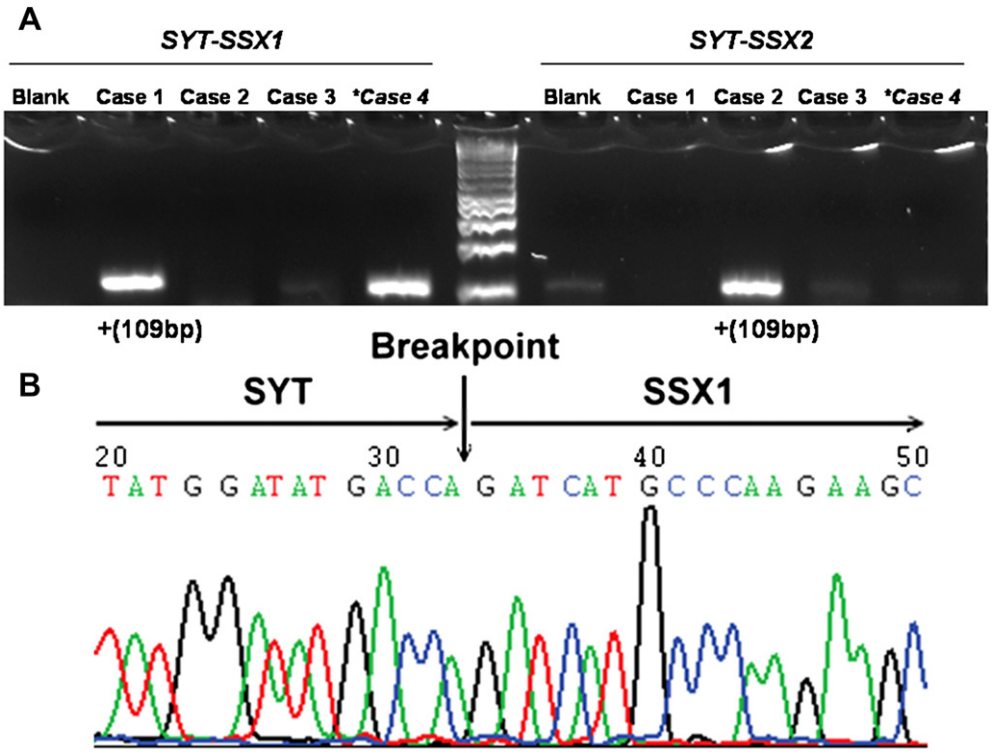

Figure 3 (A) Results of reverse transcriptase polymerase chain reaction in four cases. Case 1: positive control for *SYT—SSX1* translocation. Case 2: positive control for *SYT—SSX2* translocation. Case 3: a case of malignant peripheral nerve sheath tumor (serving as a negative control). **Case 4*: the present case. A dense band of chimeric transcript of the *SYT—SSX1* fusion gene (left part), but not *SYT—SSX2* (right part), is shown. **(B)** The fusion point of the *SYT—SSX1* gene is demonstrated with cDNA sequencing.

unusually located tumors that might have been misdiagnosed as other spindle cell tumors in the past.

Although the mainstay of treatment for synovial sarcomas is surgical resection with or without radiation therapy to enhance local control, patients with primary extremity tumors greater than 5 cm in size or metastatic lesions have been shown to benefit from adjuvant chemotherapy using an ifosfamide-based regimen.[15,16] The latter

Table 1 Clinical features and outcomes of reported cases of gastric synovial sarcoma.

Case	Age	Sex	Size (cm)	Site	Adjuvant therapy	Outcome	Reference
1	67	F	0.8	Body—antrum junction	Nil	ANED, 12 mo	Makhlouf et al[3]
2	49	M	2	Body	Nil	DOD (omental metastases), 29 mo	Makhlouf et al [3]
3	68	F	2	Body	Nil	ANED, 22 mo	Makhlouf et al [3]
4	29	M	2.8	Body	Nil	ANED, 224 mo	Makhlouf et al [3]
5	54	F	3	Antrum to gastroduodenal junction	Nil	Not provided (recent case at the time of publication)	Makhlouf et al [3]
6	58	F	3	Body	Nil	ANED, 21 mo	Makhlouf et al [3]
7	37	F	4	Fundus	Nil	Local recurrence, DOO, 48 mo	Makhlouf et al [3]
8	50	M	6	Distal fundus	Chemotherapy	AWD (recurrence), 6 mo	Makhlouf et al [3]
9	42	M	8	Body	Chemotherapy	DOD, 25 mo	Makhlouf et al [3]
10	66	F	15	Fundus	Nil	Lost to follow-up	Makhlouf et al [3]
11	55	F	16	Antrum	Nil	DOD, 6 mo	Billings et al [4]
12	38	F	7.2	Body	Chemotherapy	AWD (liver metastasis), 6 mo	Current case

ANED = alive without evidence of disease; DOD = died of disease; DOO = died of other causes; AWD = alive with disease.

indeed produced a striking short-term effect on the metastatic tumors in our case, although its general benefit in gastrointestinal cases remains to be determined. Only three cases with gastric tumors have received chemotherapy, one being the current case; the regimens in the two cases are unclear, and radiation therapy was not performed in any of the 12 patients (Table 1). Parenthetically, the relative chemosensitivity of synovial sarcomas in comparison with other sarcomas highlights the importance of accurate diagnosis of this entity.

The clinical outcome of patients with synovial sarcoma in the extremities is significantly related to tumor size and local invasion status - larger tumor size (>5 cm) and invasion of bone, nerves, or vessels are correlated with a worse prognosis.[15] The prognosticative power of tumor size also seems to hold true for the gastric counterparts, as four of the six patients with tumors smaller than 5 cm had an uneventful postoperative course, whereas none of the four patients with larger tumors did.

Conclusion

Primary synovial sarcoma of the gastrointestinal tract is rare and prone to misdiagnosis. When facing a malignant spindle cell tumor of the gastrointestinal tract, synovial sarcoma should not be neglected when listing the differential diagnoses. The use of molecular techniques such as RT-PCR to detect the pathognomonic translocation is the key to making a correct diagnosis in doubtful cases and hence providing them with adequate treatment.

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